REMARKS

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

The rejection of claims 1-20 and 25-28 under 35 U.S.C. § 112 (second paragraph) for indefiniteness is respectfully traversed in view of the above amendments.

The rejection of claims 1-6, 8-11, 16-20, and 25 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,874,260 to Cleuziat et al. ("Cleuziat") is rendered moot in view of the cancellation of those claims. However, applicants submit that new claims 29-50 are allowable over Cleuziat for the following reasons.

Cleuziat relates to a method of synthesizing a nucleic acid by cyclic amplification of a target sequence. Amplification is primed by an oligonucleotide primer containing (i) a stem and loop (or hairpin) structure at the 5' end of the oligonucleotide, which includes a blocking agent that precludes extension of a synthesized complementary strand by a polymerase; (ii) a segment capable of hybridizing to a target nucleic acid, which segment is not part of the stem; and, optionally, (iii) a segment which acts as a promoter for RNA polymerase (Cleuziat, Figure 1, col. 8, lines 33-44 and col. 11, lines 1-40). Origin of synthesis occurs at the 3' end of the oligonucleotide primer; however, the 3' end of the primer does not form any part of the stem. During initial synthesis steps (Cleuziat, Figure 4A), the oligonucleotide primer hybridizes to the target nucleic acid which is to be copied, affording strands II, II' and, subsequently, strands IV, IV'. The blocking agent allows the size of strands II, II' and then strands IV, IV' to be restricted in length, during synthesis thereof, to include a specific target sequence. Strands IV, IV' form the template for cyclic amplification (Cleuziat, Figure 4B).

In contrast to Cleuziat, the method of amplifying nucleic acid according to claim 29 presently recites "providing a first template having (i) a 3' end portion comprising a first region and a first complementary region which, under suitable conditions, anneal to one another to form a first loop, (ii) a 5' end portion comprising a second region and a second complementary region which, under suitable conditions, anneal to one another to form a second loop, and (iii) a single-stranded target region connecting the 3' end portion and the 5' end portion..." (see structure shown in Figure 2 at step (7)). Cleuziat fails to teach a template as recited, which includes stem/loop formations at both the 3' and 5' ends of the template.

The next step (step B) of claim 29 recites "synthesizing a nucleic acid chain complementary to the single-stranded target region using the 3' terminal of the first template, when the first region and first complementary region are annealed to one another, as the origin of said synthesizing." As shown in Figure 2 at step (7), the 3' terminal of the first template includes region (F1), which forms a stem structure with complementary region (F1c), and this 3' terminal serves as the origin of synthesis, indicated by the arrow. While the origin of synthesis in Cleuziat also begins at the 3' end of the primer (described above), the 3' end does not include the stem/loop structure. Thus, Cleuziat also fails to teach this aspect of the present invention.

Steps C and D of claim 29 concerns the preparation of a second template complementary to the first template which is carried out by "annealing to the first loop of the first template an oligonucleotide primer comprising at the 3' terminal a nucleotide sequence complementary to the first loop" and "extending the oligonucleotide primer along the first template...". The primer H1 in Cleuziat does not anneal to a loop portion of template IV (Cleuziat, Figure 4B). Thus, Cleuziat also fails to teach this aspect of the present invention.

Because Cleuziat fails to teach several limitations of the recited method of claim 29, Cleuziat cannot be used to reject claims 29-50.

The rejection of claims 1-11, 16-20, and 25 under 35 U.S.C. § 103(a) for obviousness over Cleuziat is rendered moot in view of the cancellation of those claims. However, applicants submit that new claims 29-50 are allowable over Cleuziat for the following reasons.

Initially, applicants wish to note that typographical errors appear at pages 10, 11, and 13 of the outstanding office action. The statutory basis of the rejection in each of paragraphs 6-8 is asserted to be 35 U.S.C. § 102(e), while paragraph 5 sets forth the requirements of 35 U.S.C. § 103(a). Pursuant to a phone conference between Examiner Chakrabarti and the undersigned attorney, applicants were apprised of the typographical errors. The asserted basis of rejection in each of paragraphs 6-8 should have been 35 U.S.C. § 103(a).

Cleuziat is cited substantially as described above. For substantially the same reasons asserted above, applicants submit that Cleuziat fails to teach or suggest each of the limitations of claim 29.

The primer in Cleuziat requires at the loop region (region "e" in Cleuziat, Figure 1) a blocking agent that terminates complementary strand synthesis (Cleuziat, Col. 6,

line 61 to Col. 7, line 5). This is depicted in Cleuziat (Figure 2), where loop region "e" contains a line drawn through the loop (line = the blocking agent), thereby causing complementary strand synthesis to terminate (without synthesizing the complementary, stem-forming region in the same strand). Owing to this, the 3' terminal of the product made using Cleuziat's primer as the template cannot form a complementary nucleotide sequence at the 3' terminal (Cleuziat, Figure 2). The termination of the complementary strand synthesis reaction by the blocking agent is a vital requirement in the method of Cleuziat. Hence, elimination of the blocking agent would destroy the operability of the primer and the cyclic synthesis scheme of Cleuziat. For this reason, Cleuziat cannot be said to teach or suggest providing a template characterized by the stem/loop formations as recited in claim 29, let alone synthesizing a second template which is complementary to the first template.

Because Cleuziat fails to teach or suggest several limitations of the method of claim 29, Cleuziat cannot be used to reject claims 29-50.

The rejection of claims 1-11, 13-20, and 25-28 under 35 U.S.C. § 103(a) for obviousness over Cleuziat in view of U.S. Patent No. 6,025,139 to Yager et al. ("Yager") is rendered moot in view of the cancellation of those claims. However, applicants submit that new claims 29-50 are allowable over Cleuziat in view of Yager for the following reasons.

Cleuziat is cited substantially as described above.

Yager relates to a ligase-based assay that utilizes a set of linear oligonucleotide probes which, when matched perfectly to a target sequence, afford a ligation product of predictable size. The U.S. Patent and Trademark Office ("PTO") cites to Yager for teaching use of betaine as a melting temperature regulator. However, Yager fails to overcome the above-noted deficiencies of Cleuziat. Therefore, Cleuziat in view of Yager cannot be used to reject claims 29-50.

The rejection of claims 1-11, 13-20, and 25-28 under 35 U.S.C. § 103(a) for obviousness over Cleuziat in view of Yager and Stratagene Catalog (1988), page 39, is rendered moot in view of the cancellation of those claims. However, applicants submit that new claims 29-50 are allowable over Cleuziat in view of Yager and the Stratagene catalog for the following reasons.

Cleuziat and Yager are cited substantially as described above.

The PTO cites to the Stratagene catalog as evidence that it would have been obvious to assemble the materials necessary for performing the claimed methods in the form

of a kit, yet the Stratagene catalog does not overcome the other deficiencies of Cleuziat alone or in combination with Yager. For these reasons, Cleuziat in view of Yager and Stratagene cannot be used to reject claims 29-50.

In view of the all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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8/14/01 — Date

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